LACHMAN CONSULTANT SERVICES, INC.
CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

1600 STEWART AVENUE, WESTBURY, NY 11590
(516) 222-6222 • FAX (516) 683-1887

March 28, 2002

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
HFA-305, Room 1061
5630 Fishers Lane
Rockville, MD 20852

CITIZEN PETITION

Dear Sir or Madam:

The undersigned submits this petition in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act and 21 CFR § 314.93, on behalf of a client, to request that the Commissioner of Food and Drugs permit the filing of an Abbreviated New Drug Application (ANDA) for a drug that has the same strength as a drug listed in FDA's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations", but differs in dosage form.

A. Action Requested

By this petition, the Commissioner of the Food and Drug Administration (FDA) is hereby requested to declare that Carisoprodol Orally Disintegrating Tablets, 350 mg, are suitable for submission as an ANDA. The Reference-Listed Drug (RLD) product on which this petition is based is Soma® (Carisoprodol) 350 mg Tablets, USP. Therefore, the petitioner requests a change from the RLD, Wallace Laboratories' Soma® Tablets, only in its dosage form (from tablet to orally disintegrating tablet).

B. Statement of Grounds

The Federal Food, Drug and Cosmetic Act provides for the submission of an ANDA for a drug product that differs in dosage form from that of the listed drug, provided the FDA has approved a petition that proposed filing such an application. A copy of the most recent Internet listing of the "Approved Drug Products with Therapeutic Equivalence Evaluations" (Orange Book), included in Attachment 1, lists the RLD, Wallace Laboratories' Soma® Tablets. The proposed drug product is an orally disintegrating form of the tablet, in the same strength as the RLD. The proposed product contains the same active ingredient as the RLD and is intended for the same route of administration. Thus, the proposed product will be labeled with the same conditions of use as the listed

02P-0138 CP1

drug and is expected to have the same therapeutic effect when used as indicated in the labeling.

A copy of the RLD labeling is included in Attachment 2. The labeling of the proposed product is expected to be the same as that for the RLD with the exception of the section denoting the manufacturer, and the change in dosage form, which will instruct the user to place the orally disintegrating tablet on the tongue, allowing it to rapidly disintegrate and be swallowed. A copy of the draft proposed package insert is provided in Attachment 3.

In support of the change in dosage form requested in this petition, the petitioner would like to point out that the Agency has previously approved ANDA suitability petitions allowing for a change in dosage form in many instances. A suitability petition was recently approved for the drug product Famotidine (Docket 00P-1422) to allow a change from a tablet to an orally disintegrating tablet. The petitioner is seeking the change in dosage form in an effort to make an alternate dosage form (rapidly disintegrating tablet) available to those individuals that may have difficulty in swallowing an intact tablet or prefer the proposed dosage form.

The petitioner is also requesting a waiver of the requirement to conduct pediatric studies in accordance with the Regulations Requiring Manufacturers to Assess the Safety and Effectiveness of New Drug and Biological Products in Pediatric Patients; Final Rule (Pediatric Final Rule) 63 FR 66632 published December 2, 1998, and the waiver requirements set forth in 21 CFR § 314.55(c). In support of the request to waive the requirement of pediatric studies, the petitioner notes that Carisoprodol carries a warning that, on rare occasion, the first dose has been followed by serious idiosyncratic symptoms that may require hospitalization. Given a warning of this nature, the petitioner believes that subjecting pediatric patients to studies would be of questionable ethics, particularly since Carisoprodol is indicated as an adjunctive therapy only for the relief of discomfort associated with painful musculoskeletal conditions. There are many pain-relief alternatives available to the pediatric population for which dosing has already been established, among them, several varieties of analgesics, including NSAIDs. In addition, Carisoprodol is included in the Physicians Desk Reference Product Category "Muscle Relaxants". In this particular category, pediatric dosing for patients six months and older has been determined for Valium® Tablets, for patients 30 days and older for Valium® Injectable, and Dantrium® Capsules has dosing information for pediatric patients over the age of five. Therefore, since there is evidence as noted in the label warning that a single dose of the drug product may pose an infrequent, but serious risk, the product is intended only as secondary therapy to other preferred treatments, and there are existing treatments available to pediatric patients, the petitioner believes a waiver of pediatric studies is reasonable and warranted under 21 CFR 314.55(c)(2)(i) and (iii) and is in accord with the intent of the pediatric rule.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR § 25.31.

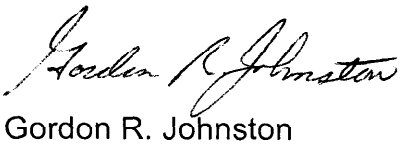
D. Economic Impact

The information will be provided upon request by the Agency.

E. Certification

The undersigned certifies, that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,



Gordon R. Johnston
Associate

GRJ/pk/m

Attachment 1: "Approved Drug Products with Therapeutic Equivalence Evaluations" (Orange Book)
Attachment 2: RLD Labeling
Attachment 3: Draft Proposed Package

cc: G Davis, OGD

71K2087

ATTACHMENT 1

Proprietary Name Search Results from "Rx" table for query on "SOMA."

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
012365	AB	Yes	ASPIRIN; CARISOPRODOL	Tablet; Oral	325MG;200MG	SOMA COMPOUND	WALLACE PHARMS
012366	AB	Yes	ASPIRIN; CARISOPRODOL; CODEINE PHOSPHATE	Tablet; Oral	325MG;200MG;16MG	SOMA COMPOUND W/ CODEINE	WALLACE PHARMS
011792	AA	Yes	CARISOPRODOL	Tablet; Oral	350MG	SOMA	WALLACE LABS

Thank you for searching the Electronic Orange Book

Return to Electronic Orange Book Home Page

ATTACHMENT 2

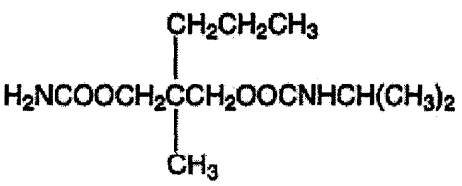
SOMA® (Wallace)

(carisoprodol)

Tablets, USP

DESCRIPTION

'SOMA' (carisoprodol) Tablets, USP is available as 350 mg round, white tablets. Chemically, carisoprodol is N-isopropyl-2- methyl-2-propyl-1,3-propanediol dicarbamate. Carisoprodol is a white, crystalline powder, having a mild, characteristic odor and a bitter taste. It is very slightly soluble in water; freely soluble in alcohol, in chloroform, and in acetone; its solubility is practically independent of pH. Carisoprodol is present as a racemic mixture. The molecular formula is $C_{12}H_{24}N_2O_4$, with a molecular weight of 260.33. The structural formula is:



Other ingredients: alginic acid, magnesium stearate, potassium sorbate, starch, tribasic calcium phosphate.

ACTIONS

Carisoprodol produces muscle relaxation in animals by blocking interneuronal activity in the descending reticular formation and spinal cord. The onset of action is rapid and effects last four to six hours.

INDICATIONS

Carisoprodol is indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomfort associated with acute, painful musculoskeletal conditions. The mode of action of this drug has not been clearly identified, but may be related to its sedative properties. Carisoprodol does not directly relax tense skeletal muscles in man.

CONTRAINDICATIONS

Acute intermittent porphyria as well as allergic or idiosyncratic reactions to carisoprodol or related compounds.

WARNINGS

Idiosyncratic Reactions --On very rare occasions, the first dose of carisoprodol has been followed by idiosyncratic symptoms appearing within minutes or hours. Symptoms reported include: extreme weakness, transient quadriplegia, dizziness, ataxia, temporary loss of vision, diplopia, mydriasis, dysarthria, agitation, euphoria, confusion, and disorientation. Symptoms usually subside over the course of the next several hours. Supportive and symptomatic therapy, including hospitalization, may be necessary.

Usage in Pregnancy and Lactation --Safe usage of this drug in pregnancy or lactation has not been established. Therefore, use of this drug in pregnancy, in nursing mothers, or in women of childbearing potential requires that the potential benefits of the drug be weighed against the potential hazards to mother and child. Carisoprodol is present in breast milk of lactating mothers at concentrations two to four times that of maternal plasma. This factor should be taken into account when use of the drug is contemplated in breast-feeding patients.
Usage in Children --Because of limited clinical experience, `SOMA' is not recommended for use in patients under 12 years of age.
Potentially Hazardous Tasks --Patients should be warned that this drug may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a motor vehicle or operating machinery.
Additive Effects --Since the effects of carisoprodol and alcohol or carisoprodol and other CNS depressants or psychotropic drugs may be additive, appropriate caution should be exercised with patients who take more than one of these agents simultaneously.
Drug Dependence --In dogs, no withdrawal symptoms occurred after abrupt cessation of carisoprodol from dosages as high as 1 gm/kg/day. In a study in man, abrupt cessation of 100 mg/kg/day (about five times the recommended daily adult dosage) was followed in some subjects by mild withdrawal symptoms such as abdominal cramps, insomnia, chilliness, headache, and nausea. Delirium and convulsions did not occur. In clinical use, psychological dependence and abuse have been rare, and there have been no reports of significant abstinence signs. Nevertheless, the drug should be used with caution in addiction-prone individuals.

PRECAUTIONS

Carisoprodol is metabolized in the liver and excreted by the kidney; to avoid its excess accumulation, caution should be exercised in administration to patients with compromised liver or kidney function.

ADVERSE REACTIONS

Central Nervous System --Drowsiness and other CNS effects may require dosage reduction. Also observed: dizziness, vertigo, ataxia, tremor, agitation, irritability, headache, depressive reactions, syncope, and insomnia. (See also Idiosyncratic Reactions under "Warnings.")
Allergic or Idiosyncratic --Allergic or idiosyncratic reactions occasionally develop. They are usually seen within the period of the first to fourth dose in patients having had no previous contact with the drug. Skin rash, erythema multiforme, pruritus, eosinophilia, and fixed drug eruption with cross reaction to meprobamate have been reported with carisoprodol. Severe reactions have been manifested by asthmatic episodes, fever, weakness, dizziness, angioneurotic edema, smarting eyes, hypotension, and anaphylactoid shock. (See also Idiosyncratic Reactions under "Warnings.")
In case of allergic or idiosyncratic reactions to carisoprodol, discontinue the drug and initiate appropriate symptomatic therapy, which may include epinephrine, antihistamines, and in severe cases corticosteroids. In evaluating possible allergic reactions, also consider allergy to excipients (information on excipients is available to physicians on request).
Cardiovascular --Tachycardia, postural hypotension, and facial flushing.
Gastrointestinal --Nausea, vomiting, hiccup, and epigastric distress.
Hematologic --Leukopenia, in which other drugs or viral infection may have been responsible, and pancytopenia, attributed to phenylbutazone, have been reported. No serious blood dyscrasias have been attributed to carisoprodol.

DOSAGE AND ADMINISTRATION

The usual adult dosage of `SOMA' (carisoprodol) Tablets, USP is one 350 mg tablet, three times daily and at bedtime. Usage in patients under age 12 is not recommended.

OVERDOSAGE

Overdosage of carisoprodol has produced stupor, coma, shock, respiratory depression, and, very rarely, death. The effects of an overdosage of carisoprodol and alcohol or other CNS depressants or psychotropic agents can be additive even when one of the drugs has been taken in the usual recommended dosage. Any drug remaining in the stomach should be removed and symptomatic therapy given. Should respiration or blood pressure become compromised, respiratory assistance, central nervous system stimulants, and pressor agents should be administered cautiously as indicated. Carisoprodol is metabolized in the liver and excreted by the kidney. Although carisoprodol overdosage experience is limited, the following types of treatment have been used successfully with the related drug meprobamate: diuresis, osmotic (mannitol) diuresis, peritoneal dialysis, and hemodialysis (carisoprodol is dialyzable). Careful monitoring of urinary output is necessary and caution should be taken to avoid overhydration. Observe for possible relapse due to incomplete gastric emptying and delayed absorption. Carisoprodol can be measured in biological fluids by gas chromatography (Douglas, J. F. et al.: *J Pharm Sci 58:* 145, 1969).

HOW SUPPLIED

`SOMA' (carisoprodol) Tablets, USP 350 mg: Round, convex, white tablets, inscribed with `SOMA' on one side and 37-WALLACE 2001 on the other side, are available in bottles of 100 (NDC 0037-2001-01) and 500 (NDC 0037-2001-03), and unit-dose packages of 100 (NDC 0037-2001-85).
Storage: Store at controlled room temperature 15°-30°C (59°-86°F).
Dispense in a tight container.

WALLACE LABORATORIES

Division of CARTER-WALLACE, INC.
Cranbury, New Jersey 08512
IN-090H2-10 Rev. 9/94

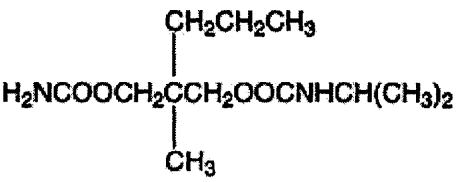
ATTACHMENT 3

Carisoprodol Orally Disintegrating Tablets

Rx Only

DESCRIPTION

Carisoprodol Orally Disintegrating Tablets are available as 350 mg tablets for oral administration. Chemically, carisoprodol is N-isopropyl-2- methyl-2-propyl-1,3-propanediol dicarbamate. Carisoprodol is a white, crystalline powder, having a mild, characteristic odor and a bitter taste. It is very slightly soluble in water; freely soluble in alcohol, in chloroform, and in acetone; its solubility is practically independent of pH. Carisoprodol is present as a racemic mixture. The molecular formula is $C_{12}H_{24}N_2O_4$, with a molecular weight of 260.33. The structural formula is:



Other ingredients: TBD

ACTIONS

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Usage in Children --Because of limited clinical experience, Carisoprodol Orally Disintegrating Tablets are not recommended for use in patients under 12 years of age.

Potentially Hazardous Tasks --Patients should be warned that this drug may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a motor vehicle or operating machinery.

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Cardiovascular --Tachycardia, postural hypotension, and facial flushing.

Gastrointestinal --Nausea, vomiting, hiccup, and epigastric distress.

Hematologic --Leukopenia, in which other drugs or viral infection may have been responsible, and pancytopenia, attributed to phenylbutazone, have been reported. No serious blood dyscrasias have been attributed to carisoprodol.

DOSAGE AND ADMINISTRATION

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OVERDOSAGE

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HOW SUPPLIED

This information will be supplied as appropriate prior to submission in an Abbreviated New Drug Application.

Storage: Store at controlled room temperature 15°-30°C (59°-86°F).
Dispense in a tight container.

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200

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SF 22

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Address 1600 STEWART AVE STE 604 Dept./Floor/Suite/Room

City WESTBURY State NY ZIP 11590

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- ☐ Yes — Shipper's Declaration not required
- ☐ Dry Ice — Dry Ice, 9, UN 1845 ____ x ____ kg

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